Application No.: 10/588,685
Attorney Docket No.: P193US
First Applicant's Name: Fabian Model
Application Filing Date: 21 June 2007
Date of Office Action: 22 January 2010
Date of Response: April 21, 2010
Examiner: Stephanie Kane Mummert

IN THE CLAIMS:

Applicants, pursuant to 37 C.F.R. § 1.121, submit the following amendments to the claims:

1. (Currently Amended) A method for producing DNA, wherein a methylation analysis is used, comprising the steps of:

   a) performing a genome-wide amplification on genomic DNA, and

   b) using the amplificates generated in step a) as a standard in the methylation analysis.

2. (Previously canceled)

3. (Previously presented) A method of claim 1 wherein the amplification methods performed are PEP, DOP-PCR or linker PCR.

4. (Previously presented) A method of claim 1 wherein the amplification method performed is a multiple displacement amplification (MDA).

5. (Previously presented) A method of claim 4, further comprising using a φ29 polymerase.

6. (Previously presented) A method of claim 4, further comprising using a commercially available kit.

7. (Previously presented) A method of claim 6, wherein the commercially available kits are "GenomiPhi" (Amersham Biosciences) or "Repli-g" (Molecular Staging).

8. (Previously presented) A method of claim 4, further comprising a commercially available DNA produced by MDA is used as a standard.

9. (Previously presented) A method of claim 1 further comprising using restriction enzymes.

10. (Previously presented) A method of claim 1 further comprising performing the methylation analysis after conversion of the DNA into a form, in which methylated cytosines can be distinguished from non-methylated cytosines by means of hybridization, by methylation-specific ligation methods, MSP, Heavy Methyl or MethyLight.

11. (Previously presented) A method claim 1 further comprising performing the methylation analysis after conversion of the DNA into a form, in which methylated cytosines can be distinguished from non-methylated cytosines by means of hybridization, by primer extension.

12. (Previously presented) A method of claim 1 further comprising performing the methylation analysis after conversion of the DNA into a form, in which methylated cytosines can be distinguished from non-methylated cytosines by means of hybridization, by an amplification and a hybridization of the amplificates at oligomer microarrays.

13. (Previously presented) A method of claim 1 further comprising performing the methylation analysis after conversion of the DNA into a form, in which methylated cytosines can be distinguished from non-methylated cytosines by means of hybridization, by means of a multiplex PCR.

14. (Previously presented) A method of claim 1 wherein a mixture of methylated and non-methylated DNA is used as a standard.

15. (Previously presented) A method of claim 1 wherein several mixtures of methylated and non-methylated DNA with different shares of methylated and non-methylated DNA are used as a standard.

16. (Previously presented) A method of claim 1 wherein the methylation analysis is performed for the diagnosis of cancer diseases or other diseases associated with a modification of the methylation status.

17. (Previously presented) A method of claim 1 wherein the methylation analysis is performed for the prognosis of desired or undesired effects of drugs and for the differentiation of cell types or tissues, or for the investigation of the cell differentiation.

18. (Previously presented) A method for the determination of methylation rates of DNA samples by means of microarrays containing CG and TG oligomers, comprising the steps of:

a) hybridizing the arrays with two calibration standards, which have defined methylation rates;

b) using the hybridization values of step a) to determine a calibration curve for use as a suitable method of calculation; and

c) determining the actual methylation rates of the investigated DNA samples by using this prepared calibration curve.

19. (Previously presented) A method according to claim 18, wherein the two calibration standards have methylation rates of 0% and 100%, respectively.

20. (Previously presented) A method according to claim 18, wherein more than two calibration standards are used, which have different methylation rates.

21. (Previously presented) A method according to claim 18, wherein the actual methylation rates are determined in a multi-stage calculation process, comprising the steps of:

a) normalizing the hybridization values, wherein methylation signals are determined,

b) normalizing the methylation signals with the aim of variance stabilization, and

c) determining the methylation rates by using the calibration standards and a suitable maximum likelihood algorithm.

22. (Previously presented) A method according to claim 21, further comprising a step prior to step a) wherein the hybridization values are corrected for the background noise inherent in the measurement method.

23-30. (Previously canceled)

31. (Previously presented) A method of claim 1, wherein the genome-wide amplification is performed by exclusively using nucleotides or nucleotide triphosphates, respectively, which are non-methylated.

32-39. (Previously canceled)